

FAST FACTS

WF 1801 - A Single Arm, Pilot Study of Ramipril for Preventing Radiation-Induced Cognitive Decline in Glioblastoma (GBM) Patients Receiving Brain Radiotherapy

ELIGIBILITY CRITERIA

1. Histologically proven diagnosis of glioblastoma or gliosarcoma (WHO grade IV) obtained at the time of a partial or gross total resection of the tumor. Patients who undergo a stereotactic needle biopsy alone are not eligible.
2. The tumor must have a supratentorial component.
3. History/physical examination within 14 days prior to enrollment
4. The patient must have recovered from the effects of surgery, postoperative infection, and other complications before enrollment.
5. Patient planning to receive brain RT, and concurrent and adjuvant temozolomide chemotherapy for 6 weeks as per standard of care therapy. Use of the Optune® (also known as Tumor Treating Fields or TTFs) device is allowed at provider discretion, but must begin after the Month 1 Post RT (10 wk) Neurocognitive-PRO assessment.
6. Study drug (Ramipril) must be given ≥ 21 days and ≤ 42 days after surgery.
7. All available brain MRI or CT imaging reports from surgery to study completion must be submitted. This includes any post-operative or pre-radiation scan reports.
8. ECOG 0, 1 or 2;
9. Age ≥ 18 ;
10. CBC/differential obtained within 14 days prior to enrollment, with adequate bone marrow function defined as follows:
 - Absolute neutrophil count (ANC) $\geq 1,500$ cells/mm³;
 - Platelets $\geq 100,000$ cells/mm³
 - Hemoglobin ≥ 10.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 10.0 g/dl is acceptable.)
11. Adequate renal function, as defined below:
 - BUN ≤ 30 mg/dl within 14 days prior to enrollment.
 - Creatinine ≤ 1.7 mg/dl within 14 days prior to enrollment.
12. Adequate hepatic function, as defined below:
 - Total Bilirubin ≤ 2.0 mg/dl within 14 days prior to enrollment.
 - ALT/AST ≤ 3 x normal range within 14 days prior to enrollment.
13. Patient must provide study specific informed consent prior to study entry.
14. Baseline potassium level less than 5.0 mEq/L. High potassium values that are thought to be a result of sample hemolysis may be repeated to determine an accurate potassium level and to determine potential study eligibility. Likewise high potassium values thought to be a result of potassium supplementation may be repeated at an appropriate time (5 half-lives after supplement discontinuation) to determine potential study eligibility.
15. Patient must be able to complete neurocognitive tests in the English language as they are not validated in other languages at this time.

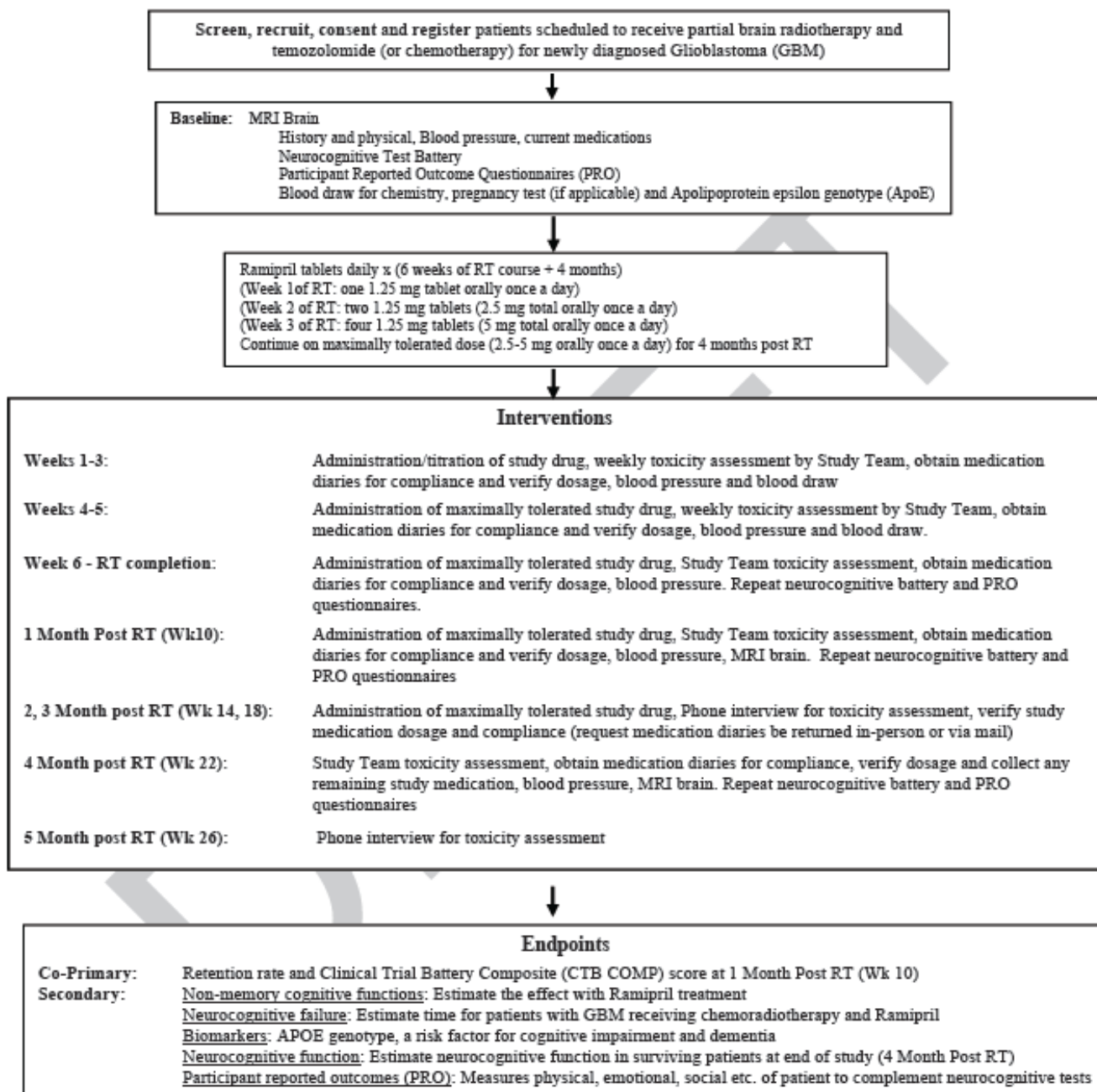
16. Women of childbearing potential and male participants must practice adequate contraception.
17. For females of child-bearing potential, negative serum or urine pregnancy test within 14 days of enrollment
18. Local site must be able to follow the standard GBM radiation treatment dosimetry plan as detailed in Section 5.1.1.2
19. For patients who will be treated with the Optune® device in addition to standard of care radiation plus concurrent and adjuvant temozolomide, the following inclusion criteria also apply:
 - Patients must have only a supratentorial glioblastoma
 - The treating physician must be a qualified provider having successfully completed the training course provided by Novocure, the device manufacturer
20. Patients with prior malignancies if all treatment for that malignancy was completed at least 2 years before registration and the patient has no evidence of disease.

EXCLUSION CRITERIA

1. Prior allergic reaction or intolerance to ACE inhibitor
2. Hypotension (less than 110mg Hg systolic) at the time of enrollment
3. Renal insufficiency with creatinine clearance of <40 ml/min (at time of enrollment)
4. Solitary kidney or known renal artery stenosis
5. Current ACE inhibitor or angiotensin receptor blocker use. Patients can come off ACE inhibitors or angiotensin receptor blockers for 1 week to be eligible for this study.
6. Prior invasive malignancy (except for non-melanomatous skin cancer) unless disease free for ≥ 2 years. (For example, carcinoma in situ of the breast, oral cavity, and cervix are all permissible).
7. Recurrent or multifocal malignant gliomas
8. Metastases detected below the tentorium or beyond the cranial vault.
9. Prior chemotherapy or radiosensitizers for cancers of the head and neck region; note that prior chemotherapy for a different cancer is allowable, except prior temozolomide. Prior use of Gliadel wafers or any other intratumoral or intracavitary treatment are not permitted.
10. Prior radiotherapy to the head or neck (except for T1 glottic cancer), resulting in overlap of radiation fields.
11. Severe, active co-morbidity, defined as follows:
 - Acute bacterial or fungal infection requiring intravenous antibiotics at the time of enrollment
 - Chronic obstructive pulmonary disease exacerbation or other respiratory illness requiring hospitalization or precluding study therapy at the time of enrollment.
 - Known HIV positivity or acquired immune deficiency syndrome (AIDS) based upon current CDC definition; note, however, that HIV testing is not required for entry into this protocol. The need to exclude patients with AIDS from this protocol is necessary because the treatments involved in this protocol may be significantly immunosuppressive.
 - Active connective tissue disorders, such as lupus or scleroderma, that in the opinion of the treating physician may put the patient at high risk for radiation toxicity.
 - Any other major medical illnesses or psychiatric impairments that in the investigator's opinion will prevent administration or completion of protocol therapy.
12. Pregnancy or women of childbearing potential and men who are sexually active and not

- willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic.
13. Pregnant or lactating women, due to possible adverse effects on the developing fetus or infant due to study drug.
 14. Patients treated on any other therapeutic clinical protocols within 30 days prior to study entry or during participation in the study unless they involve standard of care or over the counter therapies or do not involve a drug therapy. Questions regarding eligibility for patients enrolled on other therapeutic clinical trials should be forwarded to the Wake Forest NCORP Research Base email (NCORP@wakehealth.edu) for review.
 15. Patients planning to receive therapeutic antitumor agents (excluding use of the Tumor Treating Fields (TTFields or Optune®) device after the Month 1 Post RT (10 wk) Neurocognitive-PRO assessment.) in addition to standard radiation and concurrent and adjuvant temozolomide are not eligible to participate in this study.
 16. Patients with impaired decision-making capacity; this exclusion is necessary because such patients may not be able to adequately give informed consent.
 17. For patients who will be treated with the Optune® device in addition to standard of care radiation plus concurrent and adjuvant temozolomide, the following exclusion criteria also apply:
 - Optune® is not permitted in patients who have an active implanted medical device, skull defect (such as, missing bone with no replacement) or bullet fragments. Examples of active electronic devices include deep brain stimulators, spinal cord stimulators, vagus nerve stimulators, pacemakers, defibrillators, and programmaticsunts.
 - Optune® is not permitted in patients who are known to be sensitive to conductive hydrogels. Examples of conductive hydrogels are gels used on electrocardiogram (ECG) stickers or transcutaneous electrical nerve stimulation (TENS) electrodes.
 18. Patients being treated with Memantine, Donepezil, and/or other medications prescribed to enhance cognition.

SCHEMA



Study Sample: N=75
Study Duration: Approximately 26 months

Brief Eligibility Criteria: ≥ 18 years old; pathologically proven GBM; planned to receive brain RT and concurrent temozolomide chemotherapy; ECOG 0, 1 or 2; Baseline HVL-T-R Delayed Recall score must be submitted.